REMARKS

I. Pending claims

Claims 21-40 are pending and claims 1-20 have been canceled. Justification for the amendments is as follows. Amendment of the claims and the addition of new claims serve to further clarify the subject matter which applicants consider to be the invention. New claims 23-29 and 31 are drawn to polynucleotides, expression vectors, host cells, and methods of producing a polypeptide and replace original claims 3-6 and 9-14, while new claims 21-22, 30, and 35-36 are drawn to polypeptides, antibodies, and compositions comprising the polypeptide and replace claims 1-2, 15, and 16. New claims 32-34 are drawn to methods of detection of polynucleotides and replace claims 7-8. New claims 37 and 38, which are drawn to methods of identifying compounds that bind to and modulate the activity of the polypeptide, are supported in the Specification at, e.g., page 35, lines 17-29, and page 45, lines 1-7. New claims 39 and 40, drawn to methods of testing compounds for effectiveness in altering polynucleotide expression and for toxicity, are supported in the Specification at, e.g., page 30, lines 17-26, page 31, lines 17-32, page 32, lines 31-34, and page 34, lines 12-17. No new matter is added by any of these amendments.

II. Restriction Requirement

In the Restriction Requirement, the Examiner requested Applicants to elect one of the following inventions:

Group I (claims 1, 2 and 15) drawn to a protein comprising the amino acid sequence set forth in SEQ ID NO:1.

Group II (claims 3-6 and 9-14) drawn to a polynucleotide encoding a protein comprising the amino acid sequence set forth in SEQ ID NO:1, a vector, a host cell, and a process for producing the protein.

Group III (claims 7-8) drawn to a method for detecting a polynucleotide using a polynucleotide encoding a protein comprising the amino acid sequence set forth in SEQ ID NO:1.

Group IV (claim 16) drawn to an antibody against a protein comprising the amino acid sequence set forth in SEQ ID NO:1.

Group V (claim 17) drawn to an agonist to a protein comprising the amino acid sequence set forth in SEQ ID NO:1.

Group VI (claim 18) drawn to an antagonist to a protein comprising the amino acid sequence set forth in SEQ ID NO:1.

Group VII (claim 19) drawn to a method for treating or preventing a disorder by administering a protein comprising the amino acid sequence set forth in SEQ ID NO:1.

Group VIII (claim 20) drawn to a method for treating or preventing a disorder by administering an antagonist to a protein comprising the amino acid sequence set forth in SEQ ID NO:1.

Group Number	Original Claims	New Claims
Group I (claims 1, 2 and 15) drawn to a protein comprising the amino acid sequence set forth in SEQ ID NO:1.	1	21-22
	2	21-22
	15	35-36
Group II (claims 3-6 and 9-14) drawn to a polynucleotide encoding a protein comprising the amino acid sequence set forth in SEQ ID NO:1, a vector, a host cell, and a process for producing the producing the protein.	3	23-24
	4	31
	5	31
	6	31
	9	25
	10	31
	11	31
	12	26
	13	27
	14	28-29
Group III (claims 7-8) drawn to a method for detecting a polynucleotide using a polynucleotide encoding a protein comprising the amino acid sequence set forth in SEQ ID NO:1.	7	32-34
	8	34
Group IV (claim 16) drawn to an antibody against a protein comprising the amino acid sequence set forth in SEQ ID NO:1.	16	30
Group V (claim 17) drawn to an agonist to a protein comprising the amino acid sequence set forth in SEQ ID NO:1.	17	-

Group VI (claim 18) drawn to an antagonist to a protein comprising the amino acid sequence set forth in SEQ ID NO:1.	18	-
Group VII (claim 19) drawn to a method for treating or preventing a disorder by administering a protein comprising the amino acid sequence set forth in SEQ ID NO:1.	19	-
Group VIII (claim 20) drawn to a method for treating or preventing a disorder by administering an antagonist to a protein comprising the amino acid sequence set forth in SEQ ID NO:1.	20	-

Applicants hereby elect, with traverse, to prosecute Group II, (claims 23-29, and 31) drawn to a polynucleotide encoding a protein comprising the amino acid sequence set forth in SEQ ID NO:1, a vector, a host cell, and a process for producing the producing the protein (replacing original claims 3-6 and 9-14).

Applicants traverse the Restriction Requirement mailed June 26, 2003 for at least the following reasons.

The unity of invention standard ***must*** be applied in national stage applications

Section 1850 of the Manual of Patent Examining Procedure (original 8th edition, published August, 2001) (hereinafter "MPEP") provides:

> ... [W]hen the Office considers international applications ... during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111....
>
> In applying PCT Rule 13.2 to ... national stage applications under 35 U.S.C. 371, examiners should consider for unity of invention all the claims to different categories of invention in the application and permit retention in the same application for searching and/or preliminary examination, claims to the categories which meet the requirements of PCT Rule 13.2....

Id at page 1800-60 to -61.

MPEP section 1893.03(d) reiterates the Examiner's obligation to apply the Unity of Invention standard PCT Rule 13.2 instead of U.S. restriction/election of species practice:

> Examiners are reminded that unity of invention (not restriction) practice is applicable ... in national stage (filed under 35 U.S.C. 371) applications.

Id at page 1800-149, column 1.

Specific provisions of the Administrative Regulations Under the PCT and the corresponding provisions of the MPEP strongly support a finding of unity of invention among all of the claims in the present case

Unity of Invention is accepted as between claims to polypeptide sequences and claims to the polynucleotide sequences which encode them

Example 17, Part 2 of Annex B to the Administrative Instructions Under the PCT provides that unity of invention is accepted as between claims to polypeptide sequences and claims to polynucleotide sequences encoding those polypeptides. Those Examples are cited in MPEP section 1893.03(d) at page 1800-149, column 2 ("[n]ote also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions...")

Thus, in the present case, unity of invention exists at least as between claims drawn to polypeptide sequences SEQ ID NO:1 (*i.e.,* claims 21, 22, 35, and 36) and as to claims drawn to polynucleotide sequences which encode those polypeptides (*i.e.,* claims 23-26 and 31).

Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to claims 21-26, 31, 35, and 36, and examine those claims in a single application.

Unity of invention exists with respect to dependent claims in the same claim category as the independent claim from which they depend

MPEP section 1850(A) and 1893.03(d), which recite the provisions of paragraph (c) of Part 1 (entitled "Instructions Concerning Unity of Invention") of Annex B (entitled "Unity of Invention") to the Administrative Instructions Under the PCT, provides:

(A) Independent and Dependent Claims.

Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the expression "category of claim" referring

> to the classification of claims according to the subject matter of the invention claimed for example, product, process, use or apparatus or means, etc.).
>
> (i) If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention....

See MPEP section 1850(A) at page 1800-61. See also MPEP Appendix AI at page 53.

In the present case, claims 22-27, 35 and 36, all of which depend from claim 21, are directed to compositions of matter, *i.e.,* to products. All of these claims contain all of the features of the independent claim. Further, as discussed above, there is unity of invention as between claim 21 and claim 31.

Thus, it is improper to restrict claims 21, 22, 35 and 36 (replacing original claims 1, 2, and 15) from claims 23-27 and 31 (replacing original claims 3-6 and 9-13), as the Examiner has done. Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to the composition of matter claims, and that at least those claims be considered together in a single application.

Unity of invention exists as between all of Applicants' claims

MPEP 1850 provides:

> Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the contents of the claims as interpreted in light of the description and drawings. Annex B also contains examples concerning unity of invention.

Id at page 800-61.

MPEP 1893.03(d) similarly provides:

> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. For example, a corresponding technical feature is exemplified by a key defined by certain claimed structural characteristics which

> correspond to the claimed features of a lock to be used with the claimed key. Note also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions as amended July 1, 1992 contained in Appendix AI of the MPEP.

Id at page 1800-149.

In the present case, unity of invention exists among all of Applicants' claims. The claimed polypeptide sequences and the claimed polynucleotide sequences encoding them are corresponding technical features which are common to all of Applicants' claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application.

> The claimed polypeptide sequences, and the claimed polynucleotide sequences encoding those polypeptide sequences, are corresponding technical features that are common to all of Applicants' claims and that serve to technically interrelate them

Applicants' claims recite *inter alia* the polypeptide of SEQ ID NO:1, and the polynucleotides encoding this polypeptide, which sequences include the polynucleotide sequences of SEQ ID NO:2. See Table 1 of the specification. Applicants respectfully submit that the claimed polypeptide sequence of SEQ ID NO:1, and the claimed polynucleotide sequences encoding it, are corresponding technical features, given that the former are encoded by the latter, and conversely, the latter encode the former.

Further, the claimed polypeptide and corresponding polynucleotide sequences are common to all of Applicants' claims, given that each claim refers to one or both either explicitly or implicitly, by virtue of depending from a claim which makes an explicit reference to the claimed sequences.

Moreover, the claimed polypeptide and corresponding polynucleotide sequence serve to technically interrelate all of Applicants' claims. Applicants' composition of matter claims (21-27, 30, 31, 35 and 36) are drawn to either the sequences themselves (21 and 22, drawn to polypeptide sequences, and 23-25 and 31, drawn to polynucleotide sequences), to compositions of matter which comprise the sequences as one element (26-27, drawn to recombinant polynucleotide sequences and transformed cells, respectively, and 35 and 36, drawn to pharmaceutical compositions), or to

compositions of matter wherein the claimed sequences functionally limit the claimed subject matter (claim 30, drawn to antibodies which specifically bind a polypeptide of claim 21).

In Applicants' method claims (28, 29, 32-34, and 37-40), the claimed sequences serve as either the product of the claimed method (claims 28 and 29, drawn to a method of polypeptide production) and/or as a reagent for performing the method (claims 37 and 38, drawn, respectively, to methods of screening for compounds which specifically bind, or compounds which modulate the activity of, a polypeptide of claim 21; and claims 32-34, 39, and 40, drawn, respectively, to methods of detecting a target polynucleotide in a sample, a method of screening for compounds which alter the expression of a target polynucleotide, and a method for assessing toxicity of a test compound).

Therefore, the claimed polypeptide and polynucleotide sequences are corresponding technical features which are common to all of Applicants' claims, and which serve to technically interrelate them.

The claimed polypeptide and polynucleotide sequences define the contribution made by each of Applicants' claims over the prior art

Contrary to the Examiner's assertion, the polypeptide and polynucleotide sequences claimed by Applicants are themselves contributions over the prior art, and they therefore define the contribution made over the prior art by all of Applicants' other claims.

At page 3 of the Office Action currently under consideration, the Examiner alleges that since the PCT rules define a special technical feature as a feature which defines a contribution over the prior art, "...the ... claimed inventions cannot share a special technical feature with the first claimed invention," since the first claimed invention lacks novelty. The Examiner's reasoning is as follows: (1) the technical feature linking Groups I-VIII is the claimed amino acid/nucleic acid sequences; (2) the sequences disclosed by the cited reference (Morgan et al., (1996) U60116) ***allegedly*** teach polypeptide fragments of SEQ ID NO:1 and polynucleotide fragments of SEQ ID NO:2; (3) the reference sequences anticipate the claimed amino acid/nucleic acid sequences; and therefore, (4) the claimed amino acid and nucleic acid sequences lack novelty.

Applicants respectfully disagree with the Examiner's reasoning. Applicants first wish to emphasize that it is those polypeptide sequences and/or those corresponding polynucleotide sequences

in their ***entire*** form which provide the "common or corresponding special technical feature" linking all of the claims to form a single general inventive concept.

Applicants respectfully point out that the full-length polypeptide and corresponding full-length polynucleotide sequences recited in claims 21 and 31, and the claims dependent thereon, are not anticipated by the sequences described by the cited reference. First, none of the ***full-length*** polypeptide or polynucleotide sequences recited in claim 21 or claim 31 are explicitly disclosed by the cited reference. Moreover, even assuming for purposes of argument that the reference disclosed polypeptide or polynucleotide fragments which exhibit sequence identity with fragments of SEQ ID NO:1 or SEQ ID NO:2, neither SEQ ID NO:1 itself, nor any polynucleotide sequence which encodes SEQ ID NO:1, can be anticipated by those fragments. Therefore, the contribution over the prior art represented by the full-length polypeptide and polynucleotide sequences is not negated by the cited reference.

In sum, the claimed polypeptide sequences and the claimed polynucleotide sequences which encode them are corresponding technical features which are common to all of Applicants claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application. Withdrawal of the restriction requirement in the present case is therefore respectfully requested.

In the event that the Examiner does not apply the unity of invention standard to this national phase application, Applicants note that the invention encompassed by claims 32-34 (replacing claims 7 and 8 of Group III) and claims 39 and 40 are drawn to methods of use of the polynucleotides of Group II, and should be examined together. These method claims recite a product (i.e., a polynucleotide), which is of the same scope as the claimed polynucleotides being searched by the Examiner. Therefore, it would not be an undue burden on the Examiner to examine these method claims since the searches for the claimed polynucleotides and these method claims would substantially overlap.

In addition, the method claims 32-34, 39, and 40 are entitled to rejoinder upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of a product claim, for rejoinder of process claims covering the same scope of products. See also M.P.E.P. 821.04 as follows.

> Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. . . The claims to the nonelected invention will be withdrawn from further consideration under 37 C.F.R. 1.142. . . . However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 09-0108.

Respectfully submitted,

INCYTE CORPORATION

Date: July 24, 2003

Gina C. Nellesen

Gina C. Nellesen
Reg. No. 52,062
Direct Dial Telephone: (650) 843-7342

Date: July 24, 2003

Barrie D. Greene

Barrie D. Greene
Reg. No. 46,740
Direct Dial Telephone: (650) 621-7576

Customer No.: 27904
3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1-20 have been canceled.

Claims 21-40 have been added:

21. (New) An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:1,

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1,

c) a biologically active fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, and

d) an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1.

22. (New) An isolated polypeptide of claim 21 comprising the amino acid sequence of SEQ ID NO:1.

23. (New) An isolated polynucleotide encoding a polypeptide of claim 21.

24. (New) An isolated polynucleotide encoding a polypeptide of claim 22.

25. (New) An isolated polynucleotide of claim 24 comprising the polynucleotide sequence of SEQ ID NO:2.

26. (New) A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 23.

27. (New) A cell transformed with a recombinant polynucleotide of claim 26.

28. (New) A method of producing a polypeptide of claim 21, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 21, and

b) recovering the polypeptide so expressed.

29. (New) A method of claim 28, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1.

30. (New) An isolated antibody which specifically binds to a polypeptide of claim 21.

31. (New) An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising the polynucleotide sequence of SEQ ID NO:2,

b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:2,

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d).

32. (New) A method of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 31, the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

33. (New) A method of claim 32, wherein the probe comprises at least 60 contiguous nucleotides.

34. (New) A method of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 31, the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

35. (New) A composition comprising a polypeptide of claim 21 and a pharmaceutically acceptable excipient.

36. (New) A composition of claim 35, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1.

37. (New) A method of screening for a compound that specifically binds to the polypeptide of claim 21, the method comprising:

a) combining the polypeptide of claim 21 with at least one test compound under suitable conditions, and

b) detecting binding of the polypeptide of claim 21 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 21.

38. (New) A method of screening for a compound that modulates the activity of the polypeptide of claim 21, the method comprising:

a) combining the polypeptide of claim 21 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 21,

b) assessing the activity of the polypeptide of claim 21 in the presence of the test compound, and

c) comparing the activity of the polypeptide of claim 21 in the presence of the test compound with the activity of the polypeptide of claim 21 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 21 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 21.

39. (New) A method of screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 25, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,

b) detecting altered expression of the target polynucleotide, and

c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

40. (New) A method of assessing toxicity of a test compound, the method comprising:

a) treating a biological sample containing nucleic acids with the test compound,

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 31 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 31 or fragment thereof,

c) quantifying the amount of hybridization complex, and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.